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| EXAMINER | |
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| ART UNIT | PAPER NUMBER |
| 1655 | 10 |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/397,957 | Applicant(s) DUONG ET AL. | |
|---|---|---|---|
| | Examiner Frank W Lu | Art Unit 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

1)☒ Responsive to communication(s) filed on *26 March 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *11-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *See Continuation Sheet* .

## DETAILED ACTION

### *Response to Amendment*

1. Applicant's response to the office action filed on March 26, 2001 has been entered as Paper No:8. The claims pending in this application are claims 11-27. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn. The following rejections are based on amendment.

### *Drawings*

2. Applicant's request that "applicants respectively request the rejection be held in abeyance until otherwise allowable subject matter is found" has been granted by the examiner.

### *Sequence Rules Compliance*

3. The sequencing listing filed on March 26, 2001 has been enter in Paper No. 9. However, it still fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Direct the reply to the undersigned.

### *Claim Objections*

4. Claim 25 is objected to because of the following informalities: Note that "DC" is abbreviation. It can only be used after phrase appears once.

Appropriate correction is required.

***Claim Rejections - 35 U.S.C. § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 14 and 15 recite the limitation "claim 1 or 2" in the claims. There is insufficient antecedent basis for this limitation in the claim since claims 1 and 2 have been canceled.

8. The term "higher harmonic analysis " in claim 16 is a relative term which renders the claim indefinite. The term "higher harmonic analysis" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

***Response to Arguments***

In page 11, last paragraph of applicant's remarks, applicant argued that "the term 'higher harmonic signals is a term of art in the electronic field". The examiner agreed with applicant in this issue. However, it is unclear how high of a harmonic signal means a higher harmonic signal. Applicant did not give a definition for "higher harmonic signals".

***Claim Rejections - 35 U.S.C. § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

10. Claims 11 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Megerle (US Patent No. 5,874,046, filed on October 30, 1996).

Megerle teaches biological warfare agent sensor system employing ruthenium-terminated oligonucleotides complementary to target live agent DNA sequences. As shown in Figure 4, the sensor cell 12 contained a single electrode or a plurality of electrodes, depending on the specificity of identification required. In the event that the sensor system was used to identify a variety of target microorganisms, each of the synthesized modified oligonucleotides with the covalent attachment of electron donor and acceptor moieties was affixed to a separate electrode such that the sensor system contained an array of electrodes, such as the linear array 68 of oligonucleotides/electrodes. All of the electrodes in an array could be contained within the same electrolyte chamber if electrochemical means such as cyclic voltammetry, pulse polarography, and impedance measurements (see columns 6 and 14) were employed to measure the electron conductance. In the presence of the targeted microorganism, hybridization occurred between the modified oligonucleic acid and the microorganism's DNA, such that the electron conductance between the electron transfer moieties greatly increased, thereby providing a means of detecting

the presence of the target live microorganism (see abstract and third and fourth paragraphs in column 9). Note that, although Megerle did not directly show the steps (b) to (d) as described in claims 11 and 13, in the absence of convincing evidence to the contrary the claimed invention, these limitations are considered as inherent to the reference taught by Megerle since it has been known that the measurement of cyclic voltammetry includes electronic input and output signals (see Meade, US Patent No. 6,013,459, filed on June 12, 1997, columns 22-24).

Therefore, Megerle teaches the limitations recited by claims 11 and 13.

### *Claim Rejections - 35 U.S.C. § 103*

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 12, 19, 21, and 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) as applied to claims 11 and 13 above, and further in view of Meade (US Patent No. 6,013,459, filed on June 12, 1997).

The teachings of Megerle have been summarized previously, *supra*.

Megerle does not disclose: (1) the limitation recited by claims 19, 21, and 23; (2) the detection of nucleic acid using different electronic detection methods wherein an input signal comprises an alternating current component as described in claim 24 or comprises an AC component and a DC component as described in claim 25; and (3) a method of detecting target analytes in a sample comprising processing an electronic output signal to increase the signal to noise ratio as described in claim 12 or comprising an input signal with a plurality of input signals as described in claim 26 or comprising an input signal comprises the sum of multiple frequencies at a plurality of amplitudes as described in claim 27.

Meade does teach the limitations of in claims 19, 21, and 23-26 and the limitations in step (d) of claims 12 and 27 which were not taught by Megerle. He showed that electronic detection could be carried out by different methods including time or frequency dependent methods based on AD or DC current or AC voltammetry (see column 20). Note that: (1) for the teaching in processing an electronic output signal to increase the signal to noise ratio as described in claim 12, see column 21, third paragraph; (2) for the detection of nucleic acid using different electronic detection methods wherein an input signal comprises an alternating current component as described in claim 24 or comprises an AC component and a DC component as described in claim 25, see columns 20-24; (3) for an input signal with a plurality of input signals as described in claim

26 and an input signal comprises the sum of multiple frequencies at a plurality of amplitudes as described in claim 27, see columns 20 and 22-24; and (4) although Meade did not directly show that the use of a peak recognition scheme as described in claim 19, or signal average as described in claim 21, or peak recognition as described in claim 23, in the absence of convincing evidence to the contrary the claimed invention, these limitations are considered as inherent to the reference taught by Meade since these claim limitations are inherent properties of AC or DC (see Physics, principles with applications, third edition, edited by Douglas C. Giancoli, 1991, published by Prentice Hall, Englewood Cliffs, New Jersey 07632).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used different electronic detection methods suggested by Meade to detect nucleic acid hybridization because: (1) electronic detection could be carried out by different methods including time or frequency dependent methods based on AD or DC current (see Meade's patent, column 20); and (2) the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., time or frequency dependent methods based on AD or/and DC current) in the detection of nucleic acid hybridization would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known

purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

13. Claims 12, 16, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over as applied to claims 11 and 13 above, and further in view of Singhal *et al.*, (Anal. Chem. 69, 3552-3557, September 1, 1997).

The teachings of Megerle have been summarized previously, *supra*.

Megerle does not disclose a method of detecting target analytes in a sample comprising processing an electronic output signal to increase the signal to noise ratio as described in step (d) of claim 12 or the processing comprised analysis of higher harmonic signals as described in claim 16 or signal average as described in claim 21 or spectral analysis as described in claim 22.

Singhal *et al.*, do teach direct electrochemical detection of purine- and pyrimidine-based nucleotides with sinusoidal voltammetry wherein analysis process included increase electronic output signal to noise ratio (see left column in page 3555), analysis of higher harmonic signals (see Figure 2 in page 3555 and Figure 4 in page 35556), and signal averaging (see page 3554, right column, second paragraph) and spectral analysis (page 3554, left column, last paragraph).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected nucleic acid hybridization using sinusoidal voltammetry wherein analysis process included increase electronic output signal to noise ratio, analysis of higher harmonic signals, and signal averaging and spectral analysis suggested by Singhal *et al.,* because the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., sinusoidal voltammetry) in the detection of nucleic acid hybridization would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

14. Claims 12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) as applied to claims 11 and 13 above, and further in view of Cheever *et al.,* (Comput. Appl. Biosci (CABIOS), 7, 143-154, 1991).

The teachings of Megerle have been summarized previously, *supra.*

Megerle does not disclose a method of detecting target analytes in a sample comprising processing an electronic output signal to increase the signal to noise ratio as described in step (d) of claim 12 and a fast Fourier transform (FFT) analysis as described in claim 17.

Cheever *et al.,* do teach a method of detecting target analytes in a sample comprising a fast Fourier transform (FFT) analysis. FFT analysis has been a well-known algorithm from the field of signal processing and could be used for the comparison of DNA sequences by correlation (see right column of page 143 and right column of page 144) and could be traded off against signal to noise ratio as described in claim 12 (see abstract in page 143).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have been detected nucleic acid hybridization using cyclic voltammetry as suggested by Megerle and analyzed detecting signals by FFT analysis wherein analysis process included increase electronic output signal to noise ratio as suggested by Cheever *et al.*. One having ordinary skill in the art would have been motivated to modify Megerle's method and combine above methods together because FFT analysis has been a well-known algorithm from the field of signal processing (a method for standard frequency analysis, see below) and could be used in different output signal analysis (see Cheever *et al.*, right column of page 143 and right column of page 144). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to analyze the hybridization signal collected by cyclic voltammetry using FFT because all of these methods are known in the art and are easy to use.

15. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) and Cheever *et al.*, (1991) as applied to claims 11-13 and 17 above, and further in view of Wood *et al.*, (IEEE Transactions on Biomedical Engineering, 39, 730-740, 1992).

The teachings of Cheever *et al.*, and Megerle have been summarized previously, *supra*.

Cheever *et al.*, and Megerle do not disclose a method of detecting target analytes in a sample comprising joint-time frequency transformation (JTFT) analysis as described in claim 18.

Wood *et al.*, teach heart sound dynamic frequency analysis using JTFT (see abstract in page 730). Note both FFT and JTFT are standard frequency analysis techniques but may be used for different purposes (right column in page 730).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have been detected nucleic acid hybridization using cyclic voltammetry as suggested by Megerle and analyzed detecting signals by JTFT analysis as suggested by Wood *et al.*, because the simple replacement of one frequency analysis method (e.g., FFT) from another frequency analysis method (e.g., JTFT) during the process of analyzing hybridization signal would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

16. Claim 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Megerle (1996) as applied to claims 11 and 13 above, and further in view of Nederlof *et al.,* (Cytometry 13, 846-852, 1992).

The teachings of Megerle have been summarized previously, *supra.*

Megerle does not disclose a method of detecting target analytes in a sample comprising a digital filter as described in claim 20 or spectral analysis as described in claim 22.

Nederlof *et al.,* do teach a method of detecting target analytes in a sample (quantification of fluorescence *in situ* hybridization signal by image cytometry) comprising a digital filter and spectral analysis (see abstract in page 846 and pages 849-851).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected nucleic acid hybridization using image cytometry comprising a digital filter and spectral analysis suggested by Nederlof *et al.,* because the simple replacement of one electronic detection method (e.g., cyclic voltammetry) from another electronic detection method (e.g., image cytometry) in the detection of nucleic acid hybridization would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises

from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

### *Response to Arguments*

17. Applicant's arguments with respect to claims 1-10 have been considered but are moot in view of the new ground(s) of rejection.

### *Conclusion*

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. No claim is allowed.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank L., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
June 14, 2001

Ethan Whisenant, Ph.D.
Primary Examiner (FSA)